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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,400	SHOENFELD ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/8/05 has been entered.

2. Claims 14 and 28 are under consideration.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 14,19,27,28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons elaborated in the previous Office Action, paragraph 7 is withdrawn in view of the amendments to claims 14 and 28 and the cancellation of claims 19 and 27.

5. Claims 14 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "enteric coated composition" in claims 14/28. Regarding applicants comments, the specification, page 15 discloses "tablets or granules having an enteric coating", but does not disclose the scope of the claimed invention which encompasses enteric coated compositions other than a tablet or granule.

There is no support in the specification as originally filed for the recitation of "copper oxidized low density lipoprotein" in claims 14/28. Regarding the specification, page 16, said example refers to a particular LDL composition made using a particular LDL composition that was treated with copper sulfate at a specific concentration using specific reagents. The specification does not disclose the scope the claimed invention which encompasses any copper oxidized ldl wherein said term encompasses compositions made using reagents other than copper sulfate at the specific concentrations disclosed in the specification.

There is no support in the specification as originally filed for the claimed invention (the claimed inventions constitute new matter).

6. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The instant claims encompass a method that uses copper-oxidized LDL wherein the LDL is obtained from any animal species. However, there is no disclosure in the specification or prior art of LDL derived from the potentially thousands of animal species that are encompassed by the LDL recited in the claims. The prior art discloses specific forms of human LDL. Therefore, the skilled artisan cannot envision the detailed structure of the encompassed LDL molecules from any species used in the claimed method and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention

and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated peptide is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the

recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

7. Claims 14 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed method of treating atherosclerosis using copper oxidized LDL. The specification does not disclose how to use the claimed method in vivo in humans to treat disease. Applicant has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the treatment of disease in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence as to how the instant invention could be used for treating atherosclerosis using copper oxidized LDL.

Judge Lourie stated in Enzo Biochem Inc. v. Calgene Inc. CAFC 52 USPQ2d 1129 that:

The statutory basis for the enablement requirement is found in Section 112, Para. 1, which provides in relevant part that:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. . . .

35 U.S.C. Section 112, Para. 1 (1994). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " Genentech, Inc. v. Novo Nordisk, A/S , 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright , 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see Hybritech, Inc. v. Monoclonal Antibodies,

Inc. , 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), which in this case is October 20, 1983 for both the '931 and '149 patents. 8 We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., Wands , 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In In re Wands , we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See Amgen, Inc. v. Chugai Pharm. Co., Ltd. , 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Regarding Wands factors (4) and (8), the claims encompass treatment of atherosclerosis in vivo in humans. Regarding Wands factors (5) and (7), there is a high degree of unpredictability in the art. For example, Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Similarly, the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Thus, it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. Regarding Wands factor (3), while the specification provides an example in a mouse model, there were copious amounts of mouse research that suggested that oral tolerance could be used to treat MS or rheumatoid arthritis, yet said diseases were not successfully treated in humans using

oral tolerance. Regarding Wands factor (2), there is no disclosure in the specification as to what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism.
Based on the aforementioned undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification.

Regarding applicants comments and the Dorats declaration (12/8/05), Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Similarly, the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Thus, it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. Furthermore, applicants *own publication* (George et al., 2004) states (*5 years after the filing date of the instant application*) that: "The application of oral tolerance as a therapeutic strategy has proven successful in various immune and non-immune mediated *experimental models, yet efficacy in human disease is still pending*. Thus, applicants comments indicate that it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. *While the claim does not recite a specific mechanism of action, the disclosure in the specification indicates that the claimed method works via oral tolerance.* Regarding applicants comments about animal models, there were a plethora of animal models used to treat MS and RA like diseases, yet Spack teaches that attempts to treat MS in humans via inducing oral tolerance to myelin protein have been unsuccessful (see abstract) and the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Regarding Wands factor (3), while the specification provides an example in a mouse model, there were copious amounts of mouse research that suggested that oral tolerance could be used to treat MS or rheumatoid arthritis, yet said diseases were not successfully treated in humans using oral tolerance. Regarding Wands factor (2), there is no disclosure in the specification as to what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism. Regarding applicants comments, page 19 of the specification refers to

doses given to mice in a prophetic experiment for which no results were provided. Thus, it is unclear as to whether a particular dosage actually had any effect. The specification, page 18 refers to a single dosage given to mice. There is no disclosure in the specification as to dosages to be used in humans or what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism. Yesair et al. teach a composition for oral administration containing LPC (see column 5, last paragraph and Examples). LPC is also a derivative of ox ldl (see specification, page 5, first complete paragraph). LPC is a modified LDL. The specification discloses that LPC has the properties of ox ldl. The specification, page 11, fourth paragraph *discloses that LPC can be used in the previously claimed method.* Yet the Harats declaration (12/18/03) discloses that LPC and other forms of modified LDL cannot be used in the claimed method (see sections 7-9). In addition, the specification discloses that:
*"Lysophosphatidylcholine (LPC) is expressed in human atherosclerotic plaques. It is an active biological substance that can induce the first steps of atherogenesis. Indeed it is even more potent than Ox LDL."(*see page 5, penultimate paragraph).

Thus, even though LPC is involved in the pathogenesis of atherogenesis, oral tolerance to LPC cannot be used to treat atherosclerosis. Regarding the Harats declaration (12/18/03) and the LDLR mice model, Wouters et al. discloses that the LDLR mouse displays cholesterol metabolic pathways not found in humans (see page 474, second column, second paragraph)) and as a consequence "This route can serve as a backup mechanism for lipoprotein clearance in ldlr mice, yielding unforeseen side effects "(page 474, second column, first paragraph).
Regarding the various cited publications, while said publications may use the animal model under consideration, none of said publications disclose that the "likelihood of new molecules to work as anti-atherosclerosis drugs in humans is high". Furthermore, none of said publications address said model in the context of oral tolerance and the failure of animal models of oral tolerance to predict efficacy in humans. In addition, none of said publications disclose an *untested* drug that was later found to have efficacy in humans.

8. The rejection of claims 27 and 28 under 35 U.S.C. 102(b) as being anticipated by Yesair et al. (US Patent 4,874,7695) for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claim 28 and cancellation of claim 27.

9. The rejection of claims 14,19,27,28 under 35 U.S.C. 103(a) as being unpatentable over Sima et al. (11th Int. Symp. on Atherosclerosis, page 227, October 1997) and Hansson et al. (11th Int. Symp. on Atherosclerosis, page 289, October 1997)in view of Punnonen et al. (US Patent 6,541,011) is withdrawn in view of the amended claims, applicants arguments and the cancellation of claims 14 and 19.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644